UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/950,003	09/12/2001	Pasqua Oreste	MARGI 27 P1	9777

23599 7590 01/28/2003

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
KRISHNAN, GANAPATHY	
ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 01/28/2003

8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/950,003	Applicant(s) ORESTE ET AL.	
	Examiner Ganapathy Krishnan	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Specification

The priority claim should appear at the beginning of the specification. Appropriate correction is required.

Priority

Acknowledgement is made of applicant's claim for foreign priority based on an application filed in Italy on 30th March 2000. It is noted however, that the applicant has not filed a copy of the original or a certified english translation of the MI2000A000665 application as required by 35 U.S.C. 119(b).

Claim Objections

Claim 50 is objected to because of the following informalities: In Claim 50, the numeral '2,7' should be changed to '2.7'. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 11, 12, 17, 22, 33-35 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites 'N-deacetylate N-sulfate'. It is not clear if the said derivatives are N-acetylated N-desulfated or if the derivatives of K5 polysaccharide is to be N-deacetylated and N-sulfated. It is not clear what "containing from 25 to 50% on the weight of the chains" means. It is not clear what containing refers to. It is also not clear what "epimerised at least till 40% of iduronic acid with respect to total uronic acids" means.

Claim 11 recites "a tertiary or quaternary ammonium salt". It is not clear if the applicant means "a tertiary amine or a quaternary ammonium salt" and not as stated. The term tertiary is confusing.

A similar recitation is also seen in Claims 12 and 17 (iii).

Claim 17 (iv) recites 'treating a salt with an organic base of the O-oversulfated product". It is not clear what this means. It is not clear if 'a salt' refers to the salt recited in 17(iii). It is also not clear what "an organic base of the O-oversulfated product" means. It looks like the order of words recited in the claim is wrong. Claim 17 (v) and (vi) are also not clear. The recitation in 17(v) is also similar to 17(iv). Claim 17 (vi) recites 'treating the product'. It is not clear which product is referred to. A similar recitation is also seen in Claim 35 (iv-vi).

It is not clear from Claim 22 as recited if all three enzymes are used as a mixture in the said step or only one of them is used. For the purpose of prosecution of this case it is assumed that only one of the three enzymes recited is used in the said step.

Claim 33 recites 'further converted in another salt'. It is not clear what this means. The 'in' should be changed to 'into'. Also 'another salt' is not defined. A similar recitation is also seen in Claim 35 (vi).

Claim 34 recites the limitation C1C4 within parentheses. It is not clear if this limitation is part of the claim and also what it refers to. If it is part of the claim the parentheses should be removed. The claim should also state clearly what C1C4 is.

Claim 35 (iii) recites 'tertiary or quaternary salt'. It is not clear what tertiary salt means.

Claim 41 recites 'about 60% to about 55% of R, R_1, R_2 and R_3". It is not clear if percentage range quoted applies to each of the R groups or it applies to the R groups taken together. Also the numerals 60% and 55% should be switched.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-10, 14-16 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-10 and 27-29 of copending Application No. 09/738879 ('879 application). This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Joint Inventors

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11-13 and 17-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lormeau et al (USPN 5550116) in combination with Zoppetti et al (USPN 6162797) and Branellec et al (USPN 5599801).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 11-13 and 17-62 are drawn to drawn to process for preparation of glycosaminoglycans from K5 polysaccharide, which involves C5-epimerization using glucuronosyl C5 epimerase, N, O-sulfation under various conditions, glycosaminoglycans with various molecular weight ranges and percentages of hydrogens and sulfite groups and iduronic acid, their salts and pharmaceutical compositions.

Lormeau et al drawn to N,O-sulfated heparosans, teach N,O-sulfated heparans consisting of mixture of chains or mixture of chains of molecular mass between 1500 and 15,000 Daltons and their pharmaceutically acceptable salts (see col.35, line 67 through col. 36, line 23). N-acetyl heparosans in the molecular weight range of 1500-15000 Daltons are initially obtained from E coli K5 strains (col. 7, line 60 through col. 8, line 24). The heparosan obtained from natural sources have the L-iduronic acid configuration in most of the repeat units (col. 3, lines 25-45). These heparosans have repeat units in which the glucosamine moiety has acetyl groups in 0-80% of the repeat units and a hydrogen in the remaining units (col. 10, lines 1-15) and also these heparosans are useful intermediates for the preparation of the corresponding N,O-sulfated heparosans (col. 10, line 24). The N,O-sulfation is carried out via procedures known in the art (col. 10, line 34 to col. 11, line 40). Lormeau et al disclose several N,O-sulfated heparosans with different degrees of sulfation, deacetylation and molecular masses (col. 12, lines 7-50). The use of tetrabutylammonium salt is also disclosed (col. 11, lines 45-49). Lormeau discloses the preparation of various salts, all of which are pharmaceutically acceptable. Even though the use of tetrabutylammonium salt before the O-sulfation step is disclosed, this salt and the others containing alkali metal and alkaline earth metals, aluminum and zinc ions can be prepared. The

N,O-sulfated heparosans of Lormeau's invention possess good coagulation-regulatory activity (see col. 13, lines 7-8). The heparosans of Lormeau's invention also showed ATIII dependent activity (see col. 13, lines 11-41). Lormeau teaches pharmaceutical compositions in combination with one or more pharmaceutically suitable vehicles (see col. 13, lines 49-55).

Zoppetti et al teach the process steps for the preparation of the derivatives of K5 polysaccharides obtained from E coli which includes N-deacetylation, N-sulfation, C5 epimerization using epimerase and resulfation (oversulfation) (see col. 2, line 16 through col. 4, line 24 and claim 11). Therapeutic method for anticoagulant treatment of humans consisting of the administration of the polysaccharide derivatives is also disclosed (see claim 13).

However, Lormeau and Zoppetti do not teach the depolymerization of the glycosaminoglycans with nitrous acid followed by reduction with sodium borohydride.

Branellec et al drawn to amethod obtaining purified fractions of heparin, teach the depolymerization of heparin using nitrous acid followed by sodium borohydride reduction (see col. 5, lines 30-50).

Even though the teachings of Lomeau and Zoppetti do not disclose polysaccharide derivatives with limitations of instant claims 11-13 and 17-62, subsequent steps of selective desulfation, selective 6-O sulfation, the use of divalent cations in the epimerization step, doing the epimerization step with the enzyme in immobilized form, recirulating the solutions in the process of Claim 24, variations in solvent systems, concentrations and temperature over variable time periods to obtain glycosaminoglycans containing various percentages of hydrogen and sulfite groups, iduronic acid and different ranges of molecular weights and pharmaceuticals compositions are all obvious modifications that are well within the purview of a skilled artisan.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Lormeau, Zoppetti and Branellec to produce glycosaminoglycans and modifications as instantly claimed with reasonable amount of success, since the teachings of the prior art is seen to disclose the process steps for the same.

One of ordinary skill in the art would be motivated to do so since polysaccharide derivatives of the glycosaminoglycan family which have high percentages of iduronic acid are more active with respect to those containing glucuronic acid and a process which produces products having a high degree of epimerization and various degrees of sulfation could lead to enhanced anticoagulation properties. The combination of the teachings of Lormeau, Zoppetti and Branellec et al is ideal for producing such glycosaminoglycans.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 703-305-4837. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 703-308-4624. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

GK
January 26, 2003

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600